Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-126 and 129-131 were pending in this application and were rejected on various grounds. The rejections to the presently pending claims are respectfully traversed.

Claim Rejections – 35 USC § 101 and 112, first paragraph

Claims 119-126 and 129-131 are rejected under 35 U.S.C. §101 allegedly "because the claimed invention lacks a credible, specific and substantial asserted utility or a well established utility."

Claims 119-126 and 129-131 are further rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention".

The Examiner maintained rejections based on the gene amplification assay (see pages 3-6 of the Office action). Without acquiescing to the propriety of this rejection but solely in the interest of advancing prosecution in this case, and as discussed in the previous response, Applicants rely on assay 94: 'the glucose/FFA uptake assay,' for support of patentable utility of the PRO1182 polypeptide. Hence rejections directed to the gene amplification assay are considered moot.

The Examiner further rejects utility based on 'the adipocyte glucose/FFA uptake assay,' (Example 149) and says that "each of the references cited by the Applicants teaches that the agents utilized in the assays *enhance* glucose uptake by adipocyte cells, not inhibit glucose uptake..." (see page 7, lines 9-11 of Office action; emphasis added). Applicants respectfully traverse this rejection.

The art recognizes that 'the adipocyte glucose/FFA uptake assay' is an in vitro assay useful for identifying compounds with inflammatory activity in vivo

Applicants respectfully submit that inhibitors (or antagonists) to PRO1182 would *enhance* glucose uptake by adipocyte cells and one skilled in the art would easily recognize that inhibitors of the PRO1182 polypeptide, which in turn would decrease circulating FFA levels,

would be therapeutically effective in treating disorders including, but not limited to, include obesity, diabetes, and hyper- or hypo-insulinemia. Indeed, the Examiner herself acknowledges that "similar assays are commonly used to identify potential anti-diabetic agents and to examine the regulatory mechanisms of important molecules involved in fat cell metabolism" (see last line of page 7 and lines 1-3 of page 8).

The Examiner also adds that "Tafuri *et al.*, Sandouk *et al.*, Goldwaser *et al.*, Mueller *et al.* (1998) and Mueller *et al.* (2000) teach different methodologies for the measurement of glucose uptake in adipocyte cells as compared to the glucose assay of the instant specification....None of the references utilizes the stimulatory and inhibitory scale disclosed in the instant specification...the instant specification does not report any specific or statistical differences and there is no indication in the specification as to how PRO1182 inhibited glucose uptake as compared to control or whether the results were significant." Applicants respectfully disagree.

The mechanism of an asserted utility need not be understood nor need the utility be superior to other methods for attaining that utility

Applicants submit that, the fact remains that the results of the adipocyte glucose/FFA uptake assay were positive, and indicates that antagonists to PRO1182 are useful in *enhancing* glucose uptake by adipocyte cells, as discussed above. Thus, the Examiner's concern that the results were an invitation to experiment further, whether correct or incorrect, do not negate the positive results of the assay, and do not negate that description of the action of the PRO1182 polypeptides and Applicants' assertion of utility. As discussed above, one of ordinary skill in the art, in possession of these results, would have believed it more likely than not that the PRO1182 polypeptides were useful for their asserted utility.

It appears that the Examiner's concern is with regard to the underlying mechanism resulting in the positive results of the adipocyte glucose/FFA uptake assay, and not with those results themselves. However, as stated by the Federal Circuit, "it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." *In re Cortwright*, 165 F.2d 1353, 1359 (Fed. Cir. 1999). Thus, Applicants submit that such a concern is misplaced, and cannot properly form the basis of the rejections of the present claims.

Moreover, even if the Examiner's concern is also with the efficacy with which the PRO1182 polypeptides enhances glucose uptake, that is, with just *how positive* these positive results in the adipocyte glucose/FFA uptake assay were, that concern is also misplaced. The Federal Circuit has stated that "[a]n invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is not operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.* 730 F.2d 753,762, 221 U.S.P.Q. 473,480 (Fed. Cir. 1984)." *Stiftung v. Renishaw PLC* 945 F.2d 1173, 1180 (Fed. Cir. 1991).

Thus, insofar as the rejections of Claims 119-126 and 129-131 are based on concerns regarding the question or how or why the invention works, or whether there might be other molecules or methods that might better provide the asserted utility, such rejections lack a proper basis for rejection of an assertion of utility and cannot be supported. Accordingly, Applicants respectfully submit that the Examiner's comments further, fail to support a *prima facie* case of lack of utility.

One Skilled in the Art would know how to make and use the variant proteins without undue experimentation based on the teachings in the art and in the specification

As the M.P.E.P. states, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."[1] As discussed above, a considerable amount of experimentation is permissible, if it is merely routine.

Applicants submit that based on the asserted utility of antagonists of PRO1182 in enhancing glucose uptake, the disclosure in the specification, the well-established knowledge in the art (at the effective date of filing) regarding agents that modulate or regulate glucose uptake and their usefulness in treatment of metabolic diseases, one skilled in the art would have known how to make and use antagonists to the claimed PRO1182 polypeptide and would know how to use them to enhance glucose uptake. Accordingly, the Examiner is requested to reconsider and withdraw the present rejection under 35 U.S.C. §101 and §112, first paragraph.

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[1] M.P.E.P. §2164.01 citing *In re Certain Limited-charge Cell Culture Microcarriers,* 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff' sub nom. Massachusetts Institute of Technology v. A.B. Fortia,* 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985).

Claim Rejections – 35 USC § 112, first paragraph- Written Description

Claims 119-123 stand rejected under 35 U.S.C. 112, first paragraph because, according to the Examiner, the subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing." Applicants respectfully traverse this rejection.

The specification provides sufficient written description for the claimed invention:

The legal standards for evaluating Written description was discussed in the previous response. Whether the Applicants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including the level of knowledge and skill in the art, and the teaching provided by the specification. The inventor is not required to describe every single detail of his/her invention. An Applicant's disclosure obligation varies according to the art to which the invention pertains.

However, the Examiner contends that "the Applicants were not in possession of all or a significant number of polypeptides that have 80-99% homology to SEQ ID NO: 357 and still retain the function of SEQ ID NO: 357."

Applicants respectfully submit that the instant invention evidences the actual reduction to practice of full-length PRO1182 of SEQ ID NO: 357, with or without its signal sequence, or encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203088. Further the amended claims recite the functional recitation: "wherein said polypeptide inhibits the uptake of glucose or FFA (free fatty acids) by adipocyte cells," which, as discussed above, is based on a well-established assay known to the skilled artisan at the effective filing date of this application. Therefore, the polypeptides are defined both by functional as well as structural features. More recently, in *Enzo Biochem., Inc. v. Genprobe, Inc.* 296 F.3d 1316 (Fed. Cir. 2002), the court adopted the standard that "the written description requirement can be met by 'showing that the invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Id.* at 1324. While the invention in *Enzo* was still a DNA, the holding has been treated as being applicable to

proteins as well. Indeed, the court adopted the standard from the USPTO's Written Description Examination Guidelines, which apply to both proteins and nucleic acids.

Current applicable case law holds that biological sequences are not adequately described **solely** by a description of their desired functional activities. The instant claims meet the standard set by the *Enzo* court in that the claimed sequences are defined not only by functional properties, but also by structural limitations. It is well established that a **combination** of functional and structural features may suffice to describe a claimed genus. "An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."[2] Thus, the genus of polypeptides with at least 80-99% sequence identity to SEQ ID NO:357, which possess the functional property of inhibiting the uptake of glucose or FFA (free fatty acids) by adipocyte cells, would meet the requirement of 35 U.S.C. §112, first paragraph, as providing adequate written description. Accordingly, one skilled in the art would have known that Applicants had knowledge and possessed the claimed polypeptides with 80-99% sequence identity to SEQ ID NO: 357 and would further know that antagonists to PRO1182 have utility in enhancing glucose uptake. The recited property of inhibiting glucose uptake (and therefore, the property of enhancing glucose uptake by PRO1182's antagonist), adds to the characterization of the claimed polypeptide sequences in a manner that one of skill in the art could readily assess and understand.

Further, as discussed in the previous response, the instant specification provides methods for determining percent identity between two amino acid sequences. In fact, the specification teaches specific parameters to be associated with the term "percent identity" as applied to the present invention. The specification describes methods wherein the polypeptides with at least 80% identity to SEQ ID NO:357 inhibit the uptake of glucose or FFA by adipocyte cells. From the specific activity of the claimed polypeptide, the description of the claimed genus is achieved.

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[2] M.P.E.P. §2163 II(A)(3)(a)

Hence, Applicants respectfully request that this rejection under 35 U.S.C. 112, first paragraph be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney Docket No.: **39780-2730P1C33**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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